EXHIBIT 2

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF OKLAHOMA
Case No. CIV-14-665-F

RICHARD GLOSSIP, et al.,
Plaintiffs,
vs.
RANDY CHANDLER, et al.,
Defendants.

REMOTE VIDEOTAPED DEPOSITION OF
DR. JOSEPH ANTOGNINI
January 28, 2021
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Reported by:
Debra Stevens, RPR-CRR

noxious stimuli. Certainly midazolam has been used as a sole drug to induce anesthesia for a procedure, as I have mentioned in my report.

(Reporter interruption.)

A. As I mentioned in my report, there are -- I did cite studies where midazolam has been used to induce anesthesia in preparation for endotracheal intubation, which is very stimulating. And that, as I said, is in my report.

One of the challenges of using midazolam to maintain anesthesia would be that you need a very large dose to be able to achieve that, so large that nobody has actually attempted to do that for a prolonged surgical procedure.

So, if we are talking about a very short procedure, there are studies, I think, that indicate that, that you could use midazolam for painful procedures, otherwise painful procedures. But for prolonged procedures, no, there are no studies in humans where midazolam has been

used alone for the purposes I mentioned because of the massive dose that would likely need to be administered.

Q. But in humans, to use your words, such a massive dose has not been studied clinically. Correct?

A. That is correct, to my knowledge.

Q. So, you have no basis in science, in data, to opine that midazolam at any dose would maintain anesthesia. Correct?

A. I do not have any -- again, there are no data that I am aware of, any published studies where midazolam has been used by itself for a prolonged surgical procedure. By that I mean for hours and hours. So, that is correct. And that is because the dose that would be required or to even study that would be so large that it wouldn't be ethically or clinically worthwhile to pursue.

Q. So you rely upon the Gehrke reference. You mentioned endotracheal

good drug to use in the study, even the study of midazolam by itself. If they recognized midazolam by itself was not, adequate, they would have mentioned that, I would think, and they did not. The other --

Q. Did they say it was adequate?

A. That is my recollection. We can certainly pull up the reference, but that is --

Q. We'll look at it.

A. That's my recollection of it.

As far as the Miyake study is concerned, those patients received an opiate called remifentanil with the induction, and then the remifentanil was discontinued right afterwards. And that is a drug that -- its effects dissipate very, very quickly. After five, ten minutes or so or something like that, maybe shorter, the effects are gone.

So, that's one of the reasons why, if you look at how these patients behaved in terms of their

electroencephalogram, it's pretty clear that 20, 30 minutes out or more, the remifentanil is gone and that basically these patients are doing okay.

Also in the discussion section, as I recall -- we will have to pull it up. In the discussion section of the Miyake study, they talked about essentially a preliminary study, and I believe there they did not use remifentanil. So again -- and they got more or less the same result. So, that leads me to believe and opine that midazolam is sufficient to anesthetize patients for the endotracheal intubation and for the continued placement or presence of that endotracheal tube.

Q. In these cases, you said that the actual intubation takes a minute or so. Did you say that? A minute, minute and a half?

A. Yes. It can be shorter if it's an easy airway and you are skilled, or it can be a little longer. You know, somewhere around there is my guess.

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Q. Could be 30 seconds?

A. Could be 30 seconds, yes.

Q. Then it is just there for however long and then it's removed at some point. Is that fair?

A. That is correct, yes.

Q. And it could be there, you said, for days?

A. If the patient, after surgery, needs to be in an intensive care unit and needs a respirator or ventilator, yes, it could be there for days.

Q. So is it your testimony that these patients in the Miyake and Gehrke study had their tubes in for an extended period of time without any other medication but for midazolam?

A. Well, for the Miyake study that is correct. They stopped the study basically at 60 minutes. After that they basically continued on with surgery and they gave more anesthetic at that point. I don't recall exactly what they used. For the Gehrke study, I don't recall what

infusion. It's just been reported to me.

Q. Do you have an opinion as to the effect of potassium chloride on a patient at the 240 milliequivalent dose level?

A. That amount of potassium would cause pain in an awake human.

Q. What kind of pain?

A. It would be painful. I mean, patients can have significant pain from it. I have not done any type of study, of course, in terms of, you know, what level of pain it is, although I know, again, that it can be -- it is reported to be quite painful.

Q. What kind of reports are you referencing?

A. Well, I am aware of some of the reports that have been provided in the exhibits, as I recall, and just in my general knowledge. Recollection in terms of specific reports, again, I would have to refer to the ones I think that were the exhibits.

Q. So at the 10 to 40

hyperosmolar solution or blood at that point.

Q. Conceptually and in terms of a demonstrative, what happens to those cells is not dissimilar to what happens to the slug that we put salt on. Correct?

MR. MANSINGHANI: Object to form.

A. I guess that would be one way you could look at it.

Q. What pain can that cause?

A. Well, again, I already testified that potassium chloride can cause pain if it is injected into a vein. So --

Q. I am trying to understand the pathways of the pain. So you identified two. If the cells which the potassium chloride solution come in contact with act like the slug on which we put salt, how does that cause pain?

A. The nerve fibers would -- sensitive to that, I guess, in that area, they would be activated.

Q. And that would result in what

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kind of pain?

MR. MANSINGHANI: Object to form.

Q. How would you characterize that kind of pain? Where would it be felt?

A. Well, the clinical descriptions from patients are that it is a burning pain, and basically that's how it is often described.

Q. And so a 400 milliequivalent potassium chloride solution in two syringes could in essence cause the melting of the tissue in which it comes in contact with. Correct?

MR. MANSINGHANI: Object to form.

A. First off, I believe you said 400. I am not sure you meant 400. Perhaps you meant 240.

Q. I meant 240. I apologize. 240 milliequivalents. Yes.

A. I think "melting" is a bit of a pejorative term. I wouldn't say it is equivalent to melting.

withdrawal can be present during general anesthesia.

Q. If we go back to the chart, do you remember I asked you at the beginning if there were any studies you are aware of where midazolam was used as the only drug to induce and maintain anesthesia to a noxious stimuli and we identified, I think, three different kinds of procedures? One was endotracheal intubation, one was cystoscopy and one was colon -- why am I having trouble with that? What was the third one?

A. Colonoscopy.

Q. Colonoscopy. I should know that.

With respect to the colonoscopy, you can do that without anesthesia I think we established. Correct?

A. In some patients because they seem to tolerate it, but many patients don't.

Q. So is midazolam the most common, if you are using something for anesthesia,

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is midazolam the most common choice for colonoscopies?

MR. MANSINGHANI: Object to form.

A. I don't know what the most common drugs are used. If you were to say basically what percentage of colonoscopies are done with midazolam, what percentage with other drugs, I don't know the details. All I can tell you, just the total number of patients, not a percentage, a lot of them are done with midazolam and often with other drugs. But they can, based on these reports, be done on midazolam alone.

Q. Have you ever done a colonoscopy with midazolam alone?

A. I have not.

Q. How many colonoscopies have you been the anesthesiologist on?

A. My guess would be a small number. It is not something that we normally would be doing in the operating room. Occasionally we might be going up

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to the endoscopy unit to do it but it is few and far between.

Q. In terms of the level or depth of sedation on this continuum, the individuals who, in the study that you rely upon, you say got midazolam only for a colonoscopy, what level of sedation were they at?

MR. MANSINGHANI: Object to form.

A. We seem to have a bit of an internet problem here and you broke up. Can you repeat the question?

Q. Sure. And I apologize for that.

A. Probably not your fault.

Q. For the individuals who had midazolam only for anesthesia for their colonoscopy, what depth of sedation on this continuum were they at?

A. I do not recall. I have to review the study to know exactly where they had those patients at. I just don't recall.

Q. Do you have any reason to think

they were under general anesthesia?

A. I'd have to look at the study to see what level they got these patients to. I just don't know off the top of my head.

Q. Okay. With respect to the cystoscopy procedure, I think you said that is often done with local anesthesia. But in cases where midazolam was used, was midazolam used with local anesthesia or was it used alone without local anesthesia?

A. Well, in the study, at least one of the studies that I cited, they had different groups and one of the groups had midazolam alone.

Q. Okay.

A. Actually, I think it was two. Two of the four groups had midazolam alone. That is my recollection.

Q. And at what level of anesthesia in this continuum were those patients?

A. Well, again, I would have to review the study, to look at it to make sure I have got my studies in my mind

were also given muscle relaxants so they could not observe for any type of movement. But nonetheless, the responses of these patients hemodynamically were very similar across different types of drugs.

Q. And what techniques were used to evaluate those responses?

A. Heart rate and blood pressure.

Q. Have you used midazolam alone to do an endotracheal intubation?

A. My recollection is that I have. It was a long, long time ago and, I'm sorry, I just don't know -- is it possible that I could have also given an opiate? Yes, it is. I don't recall specifically.

Q. How many endotracheal intubations have you participated in?

A. Thousands. I have probably done over 10,000 anesthetics in my career, and the vast majority of those involved endotracheal intubation. So, probably talking about 6,000 maybe. It is hard to put a number on it.

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Q. So you remember on one instance using midazolam for an endotracheal intubation, but you are not sure whether or not you also used an opioid. Is that fair?

A. Yes. So, this would have been early in my career, when midazolam was just coming out for use and was being used as an induction drug. So, that is why I recall that I would have used it. We often remember, when new things come out, our experience from them. So, that is why I remember with midazolam, I remember with propofol and so forth. That's the basis for that.

Q. Have you ever used midazolam alone as the sole drug in connection with a cystoscopy?

A. No, I do not recall using it alone for cystoscopy.

Q. How many cystoscopies have you done?

A. Just to be technically correct, I have done none. I have done anesthesia

for them but I have not done them myself. But anesthesia for them, for cystoscopies, maybe hundreds. Again, it is one of those things that it is hard to put a number on. I have done a lot.

Q. Have you ever -- I have asked you about these three procedures. Have you ever used midazolam alone as a drug to induce and maintain general anesthesia?

A. I have used it, as I said, for induction. The maintenance part is one that would potentially require a large dose of a drug. To the extent that you'd have to give so much that the -- it would take a long time for a patient to wake up, that is just based on the nature of that drug. And so it would not be wise to try to maintain anesthesia with midazolam alone based on the fact that patients would take a long time to wake up.

That is an important reason why it is not done and an important reason why, in the anesthesiology field, people do not venture to try to use it as a drug

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dosages that are one-tenth of the protocol for Oklahoma on a patient that had not been intubated?

MR. MANSINGHANI: Object to form.

A. So, have I used it, even at a tenth of a dose, on a patient that has not been intubated? Do you mean that I have used it and not intubated them afterwards?

Q. Correct.

A. No.

Q. So in connection with vecuronium bromide, you always intubate the patient. Correct?

A. If you are giving vecuronium bromide, you either have -- either the patient is already intubated or you are going to intubate them. But you wouldn't give that and then walk away.

Q. And what would the sensation be of the patient who received vecuronium bromide and wasn't intubated in connection with it? What would they experience?

MR. MANSINGHANI: Object to

form.

A. This is an awake patient?

Q. A patient that was not under general anesthesia. What would they experience?

MR. MANSINGHANI: Object to form.

A. Well, again, I have to -- you know, not under general anesthesia or sedated or awake, it does make a difference. If you have somebody who is awake, then they will have the sense of losing the muscle function and they will be unable to move and then unable to breathe and then they will die.

Q. Okay. And they will experience air hunger and suffocation along the way. Correct?

A. If they are awake, yes.

Q. And how long would it take such a person to die as a result of suffocation?

A. I don't know. That is going to vary from one individual to the next

because it basically requires them to decrease their oxygen levels in their blood to the point at which they will become unconscious from the hypoxia. They would live for a little bit longer after that.

Q. So from the time that they are paralyzed to the time they become unconscious from the hypoxia, how long would that be, about?

A. We are talking about several minutes. I can't really put a number on it. It is going to depend on the individual patient.

Q. And it is your opinion that that noxious stimuli is a lesser noxious stimuli than surgical noxious stimuli?

MR. MANSINGHANI: Object to form.

A. The -- it is a little bit -- what is the word I want to use? Not a good comparison to say what is -- or to opine what are the effects of these drugs in the awake individual with no drug

may be a ceiling effect on the pain level here, so just going up a little bit more or faster may not increase the pain very much --

Q. Is that speculation, or do you have some study to --

MR. MANSINGHANI: Dr. Antognini, you froze for a bit. If you can remember, you may need to repeat the last couple sentences of what you said.

THE WITNESS: Potassium chloride is painful, but whether it is supramaximal or not, we just don't have a lot of evidence either way. You know, you might claim it is supramaximal, incredibly painful, and I am not sure that there is any good evidence out there to support that because, again, we are talking about -- you give the potassium chloride faster; does the pain go up? It may go up, but basically even at that level is it a supramaximal amount

of pain? I don't know the answer to that question.

For obvious reasons, you can -- I mean, if you did that, you would kill a patient because of the potassium overdose.

Q. Right. But we do know, at least, that clinically, if you push it, even at the lower amounts that are one-tenth of this protocol, if you push it fast, that it does in many cases cause severe pain. Correct?

MR. MANSINGHANI: Object to form.

A. Patients have reported significant pain with -- some patients have reported significant pain with potassium chloride infusion.

Q. I think you said we don't know or you don't know how much more pain is caused by the fact that we are administering ten times as much as usually is over a much shorter period of time; you just don't know how much more pain is

caused. Correct?

MR. MANSINGHANI: Object to the form and to the extent it mischaracterizes prior testimony.

A. I am not sure that anybody knows because, again, that type of administration would kill people, as we know. So, you are not going to find a lot of information out there.

Q. Do you have any basis to believe that there is a ceiling effect in terms of the pain levels for clinical administration of potassium chloride as compared to 240 milliequivalents pushed quickly?

MR. MANSINGHANI: Object to form.

A. I do not know of any clinical studies that would make that comparison, again for the same reasons I talked about. But it's possible that potassium chloride at that level, although causing pain initially, will cause enough effects on the cells and the nerve fibers that they

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are no longer able to discharge and therefore actually not function properly.

Q. Well, we know it is going to polarize the neurons that are part of the nociceptor pathway in the blood vessels. Correct?

A. Initially, that is true. But if -- and I can speculate. I mean, that is all I am doing at this point basically because I don't know that anyone studied that.

Q. So you are speculating that at some point in time the pain system stops working because of the excessive amount of potassium chloride. How long are you speculating that may take?

MR. MANSINGHANI: Object to form and to the extent it mischaracterizes prior testimony.

A. I admit what I am saying is some speculation. And I can't speculate any more because the nature of speculation is I don't have -- I am basing that opinion, speculative opinion, on my knowledge of

the effect of fluids and things like potassium chloride, how they have effects on neurons in terms of depolarizing them. Once they are depolarized, they may not work properly afterwards. Nerve fibers, I should say. But I am not aware of any data at this point that would support that speculation.

Q. So you have no scientific basis to support that speculation; and even if it were to take place at some point, you have no basis to support the speculation that it would take place before the prisoner died of a heart attack. Correct?

MR. MANSINGHANI: Object to form.

A. I do not know that, what the time frame would be relative to the cardiac arrest. All I can say is that from the moment that the potassium chloride is injected to the moment that the inmate has a cardiac arrest is going to probably be on the order of maybe 10 seconds or so.

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Q. So it might be 10 seconds of severe pain?

A. Potentially. If -- and I don't -- I should say I dispute that a prisoner in this setting would experience pain. What I am saying is that the period of the stimulation from the potassium chloride would be maybe 8 to 10 seconds before there is cardiac arrest.

And I do not -- and I believe that the inmate is not having pain because of that because of the midazolam. Midazolam, in my opinion, causes sufficient depression of the brain so that the inmate would not experience pain in the way that an awake individual would experience pain from the injection of the potassium chloride.

Q. But the adequacy of the anesthesia or the general anesthesia and the drugs used will correlate to the extent to which the stimuli are noxious. Right?

MR. MANSINGHANI: Object to

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administered a paralytic. That is the succinylcholine. Correct?

A. Yes. They were given succinylcholine. It must be on the next page where they talk about giving succinylcholine. Yes.

Q. There were no consciousness checks able to be done on these patients by virtue of the fact that they were paralyzed. Correct?

A. That is correct. You are not able to do a consciousness check after paralysis. But my point about this paper was it was a comparison between the two drugs, thiopental and midazolam. He achieved clinically adequate induction with no difference in the cardiovascular response.

Q. How soon after did they administer the additional drugs?

MR. MANSINGHANI: Object to form.

A. Additional drugs? You mean --

Q. It is highlighted here,